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SIDE CHAIN NITRATION OF POLYSUBSTITUTED 1,4-DIHYDROPYRIDINES [1]

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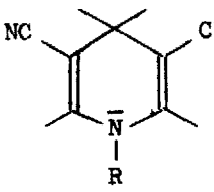
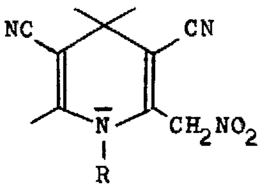
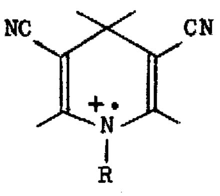
It has been reported [2,3] that polyalkylated aromatics and heteroaromatics undergo facile side chain substitutions under conditions when an electrophile is as a rule introduced on the aromatic ring. The chlorination of hexamethylbenzene to pentamethylbenzyl chloride was shown [4] to proceed via the radical-cation derived from the starting compound. An identical mechanism seems to be acceptable for other non-aromatic side chain substitutions initiated by a monoelectron transfer from the substrate to suitable electrophiles. Dihydropyridines, in contrast to analogous pyridines, are compounds of important pi-electron-rich properties [5] and might react in the mentioned way with electron with-drawing partners. As an excellent example justifying that assumption, we wish to report the easy side chain substitution of 1-benzyl-3,5-dicyano-2,4,4,6-tetramethyl-1,4-dihydropyridine (I) to the corresponding 2-nitromethyl derivative II being observed in attempts to nitrate the aromatic ring of 1-substituent.



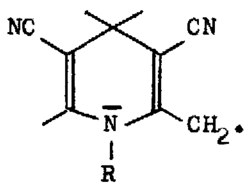
I, R = $PhCH_2$
III, R = Me



II, R = $PhCH_2$
IV, R = Me



V



VI

The dihydropyridine I reacts with nitric acid - acetic acid at 30° to 40°C or with ice-cold nitric acid - sulphuric acid to yield nitro derivative II, mp 97-8°C, having been isolated in 74 % or 81 % yields respectively.The structure

II was confirmed by a satisfactory elemental analysis and spectral data : ir ($CHCl_3$) 2205 (C≡N), 1648 and 1586 (C=C), 1568 and 1299 cm^{-1} (NO_2); pmr ($CDCl_3$) δ 1.49 (s, 6H, $(CH_3)_2C$), 2.19 (s, 3H, CH_3-C=), 4.70 (s, 2H, $-CH_2$-Ph), 5.20 (s, 2H, $-CH_2NO_2$), 6.99 to 7.40 ppm (m, C_6H_5). The mass spectrum of II showed the molecular peak to be at m/e 322 for $C_{18}H_{18}N_4O_2$.

The generality of the mentioned nitration procedure was demonstrated by the treatment of 3,5-dicyano-1,2,2,4,4,6-pentamethyl-1,4-dihydropyridine (III) with nitric acid. Fuming nitric acid (2.5 ml) was added at 20°C during 60 minutes under stirring to a solution of III (3.8 g) in chloroform (30 ml). The organic layer yielded 4.3 g (92 %) of IV, mp 149-152°C (ethanol). Ir ($CHCl_3$) 2200 (C≡N), 1648 and 1582 (C=C), 1566 and 1310 cm^{-1}(NO_2) ; pmr ($CDCl_3$) δ 1.50 (s, 6H, $(CH_3)_2C$), 2.32 (s, 3H, CH_3-C=), 3.22 (s, 3H, CH_3-N), 5.47 ppm (s, 2H, $-CH_2NO_2$). The mass spectrum of IV exhibited the molecular peak at m/e 246 for $C_{12}H_{14}N_4O_2$.

Although no intermediates were detected, we suggest that the nitration of I and III might be explained by the mechanism : I or III + $NO_2^+ \longrightarrow$ V + $NO_2^\bullet$; V $\longrightarrow$ VI + H^+ ; VI + $NO_2^\bullet \longrightarrow$ II or IV. In favour of that suggestion it may be noted that radical-cations V seem to be the key species in the electro-oxidation [1] and the mass spectrommetric fragmentation [6] of dihydropyridines I and III.

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